

Docket No.: HO-P02376US0
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Merrill A. B

Application No.: 09/514,070

Art Unit: 2729

Filed: Feb. 26, 2000

Examiner: D. SHAY

For: PHOTODYNAMIC THERAPY UTILIZING A
SOLUTION OF PHOTOSENSITIZING
COMPOUND AND SURFACTANT

APPEAL BRIEF

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-01450

Dear Sir:

As required under 37 CFR §1.192, this Appeal Brief is filed in furtherance of said Notice of Appeal.

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I. Status of the Claims

Claims 50-53 and 55-59 are pending, stand rejected, and are appealed herein. A copy of the pending claims is attached.

II. Status of the Amendments

The last claim amendments were contained within the Amendment filed on July 27, 2004.

III. Statement of Interest

The real party in interest is the sole assignee of the present application, Advanced Photodynamic Technologies, Inc.

IV. Related Appeals and Interferences

There are related appeals or interferences which would directly effect or be directed effected by or have a bearing on the Board's decision in the pending appeal. Applicant's Ser. No. 10/026,198, is a continuation in part of 09/792,578 which is a continuation in part of Ser. No. 09/514,070. Appeals have been filed in both the '578 and '198 applications and are presently pending before Examiner Shay.

V. Summary of the Invention

The present invention relates to a method of photodynamic disruption of cells, such as cancer cells, tumors and viruses. The invention includes the steps of identifying an area of cell activity and applying a concentration of a surfactant and a photosensitizing agent to the area of cell activity. The surfactant disorients cell membranes so that the membranes no longer function as an effective osmotic barrier. As a result, the photosensitizing agent is able to pass through the disoriented cell membrane. The area of cell activity is then exposed to light to cause photodynamic cellular disruption. Important to the issues at hand, the surfactant is Sodium dodecyl sulphate (SDS) provided in a solution having an SDS concentration range of between 0.003 % to 0.01%. The present invention is also directed to a method of destroying acellular organisms utilizing this same protocol.

VI. Issues on Appeal

1. Are claims 50-53 rejected under 35 U.S.C 103(a) as being unpatentable over Lai et al in combination with Singer et al.?
2. Are claims 50-53, 55 and 57-59 rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz et al in combination with Asculai et al, Singer et al, and Williams et al?
3. Is claim 56 rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz et al in combination with Asculai et al, Singer et al, and Williams et al and further in combination with Lai et al?

VII. Grouping of the Claims

- a. Regarding the §103(a) rejection based on Lai et al in combination with Singer et al, claims 50-53 stand together.
- b. Regarding the 103(a) rejection based on Swartz et al in combination with Asculai et al, Singer et al, and Williams, claims 50-53, 55 and 57-59 stand together.
- c. Regarding the 103(a) rejection based on Swartz et al in combination with Asculai et al, Singer et al, and Williams et al and Lai et al, claim 56 stands together.

VIII. Summary of the Arguments

- a. Claims 50-53 are not obvious over Lai et al combined with Singer et al. The Examiner suggests that it would have been obvious to the artisan of ordinary skill to employ SDS in the method of Lai et al, since this would aid the delivery of the pharmaceutical agent. However, Singer does not teach or suggest the claimed range of SDS for use as an aid to the delivery of pharmaceutical agents. Singer et al. discloses that SDS is frequently used to increase the absorption of relatively nonabsorbable drugs in the gastrointestinal tract and “[a]t concentrations >1% it can cause dose-related increases in the permeabilities of several organic compounds in the oral frenulum of dogs in vitro”. P.11 Singer et al proceeds to suggest that oral

pretreatment of 10% SDS significantly increased urinary recovery while pretreatment with 1% and 5% SDS "had no significant effect." P. 111.

In comparison, the SDS concentration range of the present invention is between 0.003 % to 0.01%. The significantly lower SDS concentration range of the present claims would not be "merely a matter of design choice" as the Examiner contends. While Singer et discloses that SDS within the claimed concentration may alter cell permeability, the use of SDS as a delivery aid of pharmaceuticals is at concentration ranges which are significantly greater than the claimed range. One of ordinary skill in the art would recognize that SDS concentrations of >1% can be used to facilitate pharmaceutical delivery. However, it is submitted that any proposed modification of Singer et al to lower the concentration of SDS to the presently claimed ranges would not be obvious as such a modification would change the principle of operation of the prior art invention being modified, e.g., SDS concentrations within the claimed ranges would not be useful as a delivery aid of pharmaceuticals. Furthermore, the proposed modification or combination would change the principle of operation of the prior art invention being modified as one of ordinary skill in the art would appreciate that SDS concentration of greater than the critical micellar concentration would be used to facilitate pharmaceutical delivery. The Examiner has merely selected elements identified in the various references to end up with Applicant's claimed invention. The obviousness rejection is not based on a motivation provided by the references as required under 35 U.S.C. §103(a), but is instead based on impermissible hindsight reasoning.

The Examiner's use of hindsight reasoning is evident by the suggestion that "[f]urther the inclusion of SDS in the method of Lai et al will inherently disorient the cell membrane and similarly the photosensitizer of Lai et al will pass there through. As the disorienting and passing are inherent in the use of SDS, it is not necessary that either reference recognize or rely on the effect, the steps still occur, as already set forth in the previous rejection." (emphasis added). Such a retrospective view of inherency is "not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *In re Newell*, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir 1989), cert denied, 493 U.S. 814 (1989).

b. Claims 50-53, 55 and 57-59 are not obvious over Swartz in combination with Asculai, Singer and Williams. Swartz et al discloses a system and process for generating singlet oxygen,

hydrogen peroxide and hydroxyl free radical (OH) to damage to viruses. The method includes providing a solution containing oxygen and a light reactive component, such as methylene blue. An important object of Swartz is the provision of a system capable of generating hydrogen peroxide (H^2O^2).

It is well known that SDS, an ionic detergent confers a net negative charge on molecules, proteins, viruses, etc. thereby overcoming any intrinsic charge. It is further submitted that SDS is highly reactive with strong oxidizers, such as hydrogen peroxide. Given the reactivity of SDS and hydrogen peroxide and hydroxyl free radicals, it is submitted that the addition of SDS to Swartz would not have been obvious to one of ordinary skill in the art.

Furthermore, the claimed range of SDS of the present invention would have been nonobvious. Singer et al. discloses that SDS is frequently used to as a pharmaceutical to increase the absorption of relatively nonabsorbable drugs in the gastrointestinal tract and “[a]t concentrations >1% it can cause dose-related increases in the permeabilities of several organic compounds in the oral frenulum of dogs in vitro”. P.11 Singer et al proceeds to suggest that oral pretreatment of 10% SDS significantly increased urinary recovery while pretreatment with 1% and 5% SDS “had no significant effect.” P. 111. In comparison, the SDS concentration range of the present invention is between 0.003 % to 0.01%. The significantly lower SDS concentration range of the present claims would not be “merely a matter of design choice” as the Examiner contends. While Singer et al discloses that SDS within the claimed concentration may alter cell permeability, the use of SDS as a delivery aid of pharmaceuticals is at concentration ranges which are significantly greater than the claimed range. One of ordinary skill in the art would recognize that SDS concentrations of >1% can be used to facilitate pharmaceutical delivery. However, it is submitted that any proposed modification of Singer et al to lower the concentration of SDS to the presently claimed ranges would not be obvious as such a modification would change the principle of operation of the prior art invention being modified, e.g., SDS concentrations within the claimed ranges would not be useful as a delivery aid of pharmaceuticals. Furthermore, the proposed modification or combination would change the principle of operation of the prior art invention being modified as one of ordinary skill in the art would appreciate that SDS concentration of greater than the critical micellar concentration would be used to facilitate pharmaceutical delivery. The Examiner has merely selected elements

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The Examiner fails to disclose any motivation or suggestion to combine Singer with Swartz. The Examiner's naked assertion that "Singer et al teach that SDS permiabilizes membranes greatly at concentrations below that at which total lysis occurs" does not provide a teaching or motivation to combine Singer et al with Swartz. As with the above rejections, such a retrospective view of inherency is "not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *In re Newell*, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir 1989), cert denied, 493 U.S. 814 (1989).

c. Claim 56 is not obvious over Swartz in combination with Asculai and Williams and Lai. The combination of Swartz, Asculai, Williams and Lai, even if proper, would fail to yield the step of applying a concentration including SDS to the area of cell activity. None of these references teach or disclose the use of SDS. Even if Singer et al was used by the Examiner, which it was not, for the reasons identified above with reference to claims 50-53, 55 and 57-59 above, it is submitted that this rejection of claim 56 would still be improper. There is no suggestion or motivation to modify any of these references to include the surfactant, SDS.

IX. Arguments

A. *Standard of Review*

Findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the *Administrative Procedure Act*, 5 U.S.C. §706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *In re Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312. Accordingly, the Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. Rejections Under 35 U.S.C. §103

Claims 50-53 are rejected under 35 U.S.C 103(a) as being unpatentable over Lai et al in combination with Singer et al.

The “mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.” M.P.E.P. § 2143.01; *See also, In re Mills*, 916 F.2d 680, 682, U.S.P.Q. 2d 1430, 1432 (Fed. Cir. 1990). The Examiner suggests that “[i]t would have been obvious to the artisan of ordinary skill to employ SDS in the method of Lai et al, since this would aid the delivery of the pharmaceutical agent.” However, Singer does not teach or suggest the claimed range of SDS for use as an aid to the delivery of pharmaceutical agents. Singer et al. discloses that SDS is frequently used to increase the absorption of relatively nonabsorbable drugs in the gastrointestinal tract and “[a]t concentrations >1% it can cause dose-related increases in the permeabilities of several organic compounds in the oral frenulum of dogs in vitro”. P.11 Singer et al proceeds to suggest that oral pretreatment of 10% SDS significantly increased urinary recovery while pretreatment with 1% and 5% SDS “had no significant effect.” P. 111.

In comparison, the SDS concentration range of the present invention is between 0.003 % to 0.01%. The significantly lower SDS concentration range of the present claims would not be “merely a matter of design choice” as the Examiner contends. While Singer et al discloses that SDS within the claimed concentration may alter cell permeability, the use of SDS as a delivery aid of pharmaceuticals is at concentration ranges which are significantly greater than the claimed range. One of ordinary skill in the art would recognize that SDS concentrations of >1% can be used to facilitate pharmaceutical delivery. However, it is submitted that any proposed modification of Singer et al to lower the concentration of SDS to the presently claimed ranges would not be obvious as such a modification would change the principle of operation of the prior art invention being modified, e.g., SDS concentrations within the claimed ranges would not be useful as a delivery aid of pharmaceuticals. Furthermore, the proposed modification or combination would change the principle of operation of the prior art invention being modified as one of ordinary skill in the art would appreciate that SDS concentration of greater than the critical micellar concentration would be used to facilitate pharmaceutical delivery. The

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The Examiner's use of hindsight reasoning is also evident by the statement that [f]urther the inclusion of SDS in the method of Lai et al will inherently disorient the cell membrane and similarly the photosensitizer of Lai et al will pass there through. **As the disorienting and passing are inherent in the use of SDS, it is not necessary that either reference recognize or rely on the effect, the steps still occur,** as already set forth in the previous rejection." (emphasis added). Such a retrospective view of inherency is "not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *In re Newell*, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir 1989), cert denied, 493 U.S. 814 (1989).

Claims 50-53, 55 and 57-59 were rejected under 35 U.S.C. §103(a) as being unpatentable over Swartz et al in combination with Asculai et al, Singer et al, and Williams et al.

Swartz et al discloses a system and process for generating singlet oxygen, hydrogen peroxide and hydroxyl free radical (OH) to damage to viruses. The method includes providing a solution containing oxygen and a light reactive component, such as methylene blue. An important object of Swartz is the provision of a system capable of generating hydrogen peroxide (H^2O^2). Col. 3, lines 36-37. "An important aspect of the invention is that of activating oxygen to its excited electronic and electrically reducible states to provide singlet oxygen...and hydrogen peroxide. Col. 4, lines 45-51. Swartz discloses an applied electric field between a cathode and anode to produce hydrogen peroxide via an electroreduction process. Col. 5, line 30 through Col. 6, line 59, and FIGS. 1 and 3.

It is well known that SDS, an ionic detergent confers a net negative charge on molecules, proteins, viruses, etc. thereby overcoming any intrinsic charge. It is further submitted that SDS is highly reactive with strong oxidizers, such as hydrogen peroxide. Material Safety Data Sheets

for SDS disclose the incompatibility of purified SDS and strong oxidants, such as hydrogen peroxide.

Given the reactivity of SDS and hydrogen peroxide and hydroxyl free radicals, it is submitted that the addition of SDS to Swartz would not have been obvious to one of ordinary skill in the art.

Furthermore, the claimed range of SDS would have been nonobvious. The "mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. § 2143.01; See also, *In re Mills*, 916 F.2d 680, 682, U.S.P.Q. 2d 1430, 1432 (Fed. Cir. 1990).

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The Examiner failed to disclose any motivation or suggestion to combine Singer with Swartz. The Examiner's naked assertion that "Singer et al teach that SDS permeabilizes membranes greatly at concentrations below that at which total lysis occurs" does not provide a teaching or motivation to combine Singer et al with Swartz. As with the above rejections, such a retrospective view of inherency is "not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *In re Newell*, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir 1989), cert denied, 493 U.S. 814 (1989).

Claim Rejection: 35 U.S.C. §103 –Swartz Asculai Williams Lai

Claim 56 was rejected under 35 U.S.C. §103(a) as being unpatentable over Swartz et al in combination with Asculai et al and Williams et al as applied to claims 50-53, 55 and 57-59 above, and further in view of Lai et al.

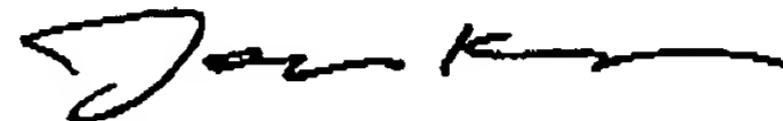
The combination of Swartz, Asculai, Williams and Lai, even if proper, would fail to yield the step of applying a concentration including SDS to the area of cell activity. None of these references teach or disclose the use of SDS. Even if Singer et al was used by the Examiner, which it was not, for the reasons identified above with reference to claims 50-53, 55 and 57-59 above, it is submitted that this rejection of claim 56 would still be improper. There is no suggestion or motivation to modify any of these references to include the surfactant, SDS. Reconsideration of this rejection is requested.

Reconsideration of these rejections is requested.

X. Conclusion

In light of the foregoing, appellant respectfully submits that all pending claims are patentable. Therefore, it is respectfully requested that the Board reverse each of the pending rejections.

Respectfully submitted,



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Date: November 7, 2005

APPENDIX 1: LISTING OF CLAIMSListing of Claims:

1 – 49 (canceled)

50. (previously amended) The method of photodynamic disruption of cells of claim 53 wherein the step of identifying an area of cell activity includes an examination of a portion of a living body.

51. (previously amended) The method of photodynamic disruption of cells of claim 53 wherein the light wavelength ranges from about 400 nm to about 800 nm, the light dosage ranges from about 10 J/cm² to about 100 J/cm² and the light dosage rate ranges from about 50 mw/cm² to about 200 mw/cm².

52. (previously amended) The method of photodynamic disruption of cells of claim 53 wherein the wavelength ranges from about 600 nm to about 700 nm.

53. (previously amended) A method of photodynamic disruption of cells comprising the steps of:

identifying an area of cell activity;

applying a concentration including a combination of a surfactant and a photosensitizing agent to the area of cell activity, said surfactant disorienting a cell membrane so that said membrane no longer functions as an effective osmotic barrier, and so that said photosensitizing agent is able to pass through the disoriented cell membrane; and

exposing the area of cell activity to light having a light wavelength, light dosage and a light dosage rate to cause photodynamic cellular disruption, wherein the surfactant is SDS provided in a solution having an SDS concentration range of between 0.003 % to 0.01%.

54. (canceled)

55. (previously amended) The method of photodynamic disruption of acellular organisms of claim 58, wherein the step of identifying an area of acellular organism activity includes an examination of a portion of a living body.

56. (previously amended) The method of photodynamic disruption of acellular organisms of claim 58, wherein the light wavelength ranges from about 400 nm to about 800 nm, the light dosage ranges from about 10 J/cm² to about 100 J/cm² and the light dosage rate ranges from about 50 mw/cm² to about 200 mw/cm².

57. (previously amended) The method of photodynamic disruption of acellular organisms of claim 58 wherein the wavelength ranges from about 600 nm to about 700 nm.

58. (previously amended) A method of photodynamic disruption of acellular organisms comprising the steps of:

identifying an area of acellular organism activity;

applying a concentration including a combination of a surfactant and a photosensitizing agent to the area of acellular organism activity, said surfactant disorienting an acellular organism membrane so that said membrane no longer functions as an effective osmotic barrier, and so that said photosensitizing agent is able to pass through the disoriented acellular organism membrane; and

exposing the area of acellular organism activity to light having a light wavelength, light dosage and a light dosage rate, wherein the surfactant is SDS provided in a solution having an SDS concentration range of between 0.003 % to 0.01%.

59. (previously amended) The method of photodynamic disruption of acellular organisms of claim 58 wherein the step of identifying an area of acellular activity includes the step of identifying an area of virus activity.

60 – 102 (canceled)